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The P2Y(1) receptor closes the N-type Ca(2+) channel in neurones, with both adenosine triphosphates and diphosphates as potent agonists.

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The rat P2Y(1) nucleotide receptor, the P2Y subtype abundant in the brain, was heterologously expressed in rat superior cervical ganglion neurones by micro-injection of the receptor cRNA or cDNA. ADP inhibited the N-type Ca(2+) current by 64%, with EC(50) 8.2 nM, an action blocked competitively by the P2Y(1) receptor antagonist adenosine 3', 5'-bisphosphate (K(i) 0.7 microM). 2-Methylthio-ADP inhibited the Ca(2+) current likewise, but with EC(50) 0.57 nM, giving the highest potency reported therewith for P2Y(1). Significantly, ATP and 2-methylthio-ATP were also agonists, the latter again at a very high potency (EC(50) 2.5 nM). We propose that this neuronal receptor, when present in brain at a high density as at synapses, can respond to very low concentrations of ATP and ADP as agonists, and that this would result in inhibition of N-type Ca(2+) currents and hence can reduce transmitter release or increase neuronal excitability.

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